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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/762,154	01/21/2004	Jun-Ichi Nezu	14875-057002 / C2-906DP1P	4898

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EXAMINER	
BUNNER, BRIDGET E	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 08/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/762,154	NEZU ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-27* is/are pending in the application.

4a) Of the above claim(s) *26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-25 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *8-27* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 May 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/521,195.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/21/04; 2/19/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Appendices A,B,C*.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, claims 8-25 and 27, drawn to an isolated nucleic acid encoding the polypeptide of SEQ ID NO: 1, vector, host cell, and method of making the polypeptide in the reply filed on 12 June 2006 is acknowledged.

Claim 26 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 12 June 2006.

Claims 8-25 and 27 are under consideration in the instant application.

Sequence Compliance

1. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). **Specifically, the sequences disclosed in Figure 3 are not accompanied by the required reference to the relevant sequence identifiers.** This application fails to comply with the requirements of 37 CFR 1.821 through 1.825. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825).

Specification

The disclosure is objected to because of the following informalities:

2. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (see pg 12, line 20). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

3. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: "POLYNUCLEOTIDES ENCODING hOCTN1 POLYPEPTIDE".

Appropriate correction is required.

35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 12, 20, and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Claims 12, 20, and 25 are rejected as being indefinite because the claims recite that the nucleic acid of claim 11 encodes a polypeptide that is a transporter of an organic cation. However, claim 11, line 3 recites a nucleic acid sequence that is the complement of SEQ ID NO: 2. It is not clear how the polynucleotide complement of SEQ ID NO: 2 produces the polypeptide disclosed in the instant application. A complement is a sequence of nucleotide bases in one strand of a DNA or RNA molecule that is exactly complementary (adenine-thymine, adenine-uracil, or guanine-cytosine) to that on another single strand.

Claim Rejections - 35 USC § 101 and 35 USC § 112, first paragraph

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 8-25 and 27 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility. Novel biological molecules lack well established utility and must undergo extensive experimentation.

The claims are directed to an isolated nucleic acid encoding a polypeptide comprising an amino acid sequence at least 70% identical to SEQ ID NO: 1, wherein the polypeptide is a transporter of an organic cation. The claims are also directed to an isolated nucleic acid encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 1, with up to 30 consecutive amino acid substitutions, wherein the polypeptide is a transporter of an organic cation. The claims recite an isolated nucleic acid comprising a strand that hybridizes under stringent conditions to a single stranded probe, the sequence of which consists of SEQ ID NO: 2 or the complement. The claims recite the strand is at least 15 nucleotides long. The claims also recite vectors, cultured host cells, and a method of producing a polypeptide.

The specification discloses that a fetal gene library is screened and an unknown gene showing significant homology to organic cation transporters is discovered (pg 4, lines 22-30). The putative transporter, termed OCTN1, is strongly expressed in kidney, bone marrow, trachea, and fetal liver and weakly detected in skeletal muscle, lung, placenta, prostate, spleen, spinal cord, and fetal kidney and lung (pg 24, lines 1-18; Figure 2). The specification also discloses that OCTN1 is expressed in several tumor cell lines (pg 24, lines 18-21). The specification

teaches that OCTN1 transports TEA, carnitine, mepyramine, quinidine, actinomycin D, etoposide, vinblastine, daunomycin (pg 18, lines 1-19; Figures 5-11). Additionally, relevant post-filing date art only teaches that OCTN1 is a polyspecific transporter that has a preference for organic cations (Koepsell et al. Rev Physiol Biochem Pharmacol 150: 36-90, 2003, especially pg 67; Koepsell et al. Eur J Physiol 447: 666-676, 2003, especially pg 671). However, the instant specification and the post-filing date art do not teach any physiological significance or functional characteristics of the OCTN1 polynucleotide (SEQ ID NO: 2) or polypeptide (SEQ ID NO: 1). The specification also does not disclose any methods or working examples that indicate the polynucleotides and polypeptide of the instant invention are involved in any specific activity. There is no biological activity, phenotype, disease or condition, binding partner, or any other specific feature that is disclosed as being associated with OCTN1. Without any information as to the specific properties of OCTN1, the mere identification of the polypeptide is not sufficient to impart any particular utility to the claimed polynucleotides. Since significant further research would be required of the skilled artisan to determine how the claimed polynucleotide and polypeptide are involved in any activities, the asserted utilities are not substantial. Since the utility is not presented in mature form and significant further research is required, the utility is not substantial. The specification asserts the following as patentable utilities for the claimed putative OCTN1 nucleic acid (SEQ ID NO: 2):

1) to design drugs that would improve transport and absorbability mediated by the transporter (pg 14, lines 18-24).

2) for gene therapy (pg 15, lines 14-31; pg 16, lines 1-4)

3) to develop carcinostatics that would be readily absorbed by the transporter (pg 16, lines 14-16)

4) to design an antisense DNA oligonucleotide (claim 15)

Each of these shall be addressed in turn.

1) to design drugs that would improve transport and absorbability mediated by the transporter. This asserted utility is not specific or substantial. Such assays can be performed with any polypeptide and nucleic acid. Nothing is disclosed about how the transporter or a specific function of the transporter is affected by the drugs. Additionally, the specification discloses nothing specific or substantial for the drugs designed in this method. Since this asserted utility is also not presented in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

2) for gene therapy. This asserted utility is not specific or substantial. Such can be performed for any nucleic acid. Further, the specification does not disclose diseases associated with a mutated, deleted, or translocated OCTN1 gene (SEQ ID NO: 2). Significant further experimentation would be required of the skilled artisan to identify individuals with such a disease. Since this asserted utility is also not presented in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

3) to develop carcinostatics that would be readily absorbed by the transporter. This asserted utility is not specific or substantial. Such assays can be performed with any polypeptide and nucleic acid. Nothing is disclosed about how the transporter or a specific function of the transporter is affected by the carcinostatics. Additionally, the specification discloses nothing specific or substantial for the carcinostatics developed in this method. Since this asserted utility is also not presented in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

4) to design an antisense DNA oligonucleotide. This asserted utility is not specific or substantial. Antisense oligonucleotides can be designed from any polynucleotide sequence. Further, the specification does not disclose a specific DNA target. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

It is clear from the instant specification that the OCTN1 transporter polypeptide described therein is what is termed an "orphan protein" in the art. This is a protein whose cDNA has been isolated because of its similarity to known proteins. There is little doubt that, after complete characterization, this DNA and protein, may be found to have a specific and substantial asserted utility. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is

> insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

7. Claims 8-25 and 27 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

7a. However, even if the claimed invention is eventually deemed to have a specific and substantial asserted utility or a well established utility, claims 8, 10-12, 14-16, 18-21, 23-25, and 27 would remain rejected under 35 U.S.C. § 112, first paragraph. Specifically, the specification of the instant application teaches that mutant proteins obtained by altering the amino acid sequence of the transporter protein by substitution, deletion, or addition of amino acid residues and are functionally equivalent to those transporter proteins of the invention are included in the invention (pg 9, lines 22-27). However, the specification does not teach any variant, fragment, or derivative of the hOCTN1 polypeptide other than the full-length amino acid sequence of SEQ ID NO:1. The specification also does not teach any variant, fragment, or derivative of the hOCTN1 nucleic acid other than the full-length nucleic acid sequence of SEQ ID NO: 2. The specification also does not teach functional or structural characteristics of the polynucleotide polypeptide variants, fragments, and derivatives recited in the claims.

The problem of predicting protein and DNA structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and DNA is extremely complex. While it is known that many amino acid substitutions are generally

possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the DNA and protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone (Bork, 2000, Genome Research 10:398-400; Skolnick et al., 2000, Trends in Biotech. 18(1):34-39, especially p. 36 at Box 2; Doerks et al., 1998, Trends in Genetics 14:248-250; Smith et al., 1997, Nature Biotechnology 15:1222-1223; Brenner, 1999, Trends in Genetics 15:132-133; Bork et al., 1996, Trends in Genetics 12:425-427).

Additionally, the art contains numerous examples of transporter families whose members

have high homologies yet disparate functions. For example, Bisson et al. (Crit Rev Biochem Mol Biol 28 : 259-308, 1993) studied yeast transporter knockout phenotypes and found little correlation between homology and the substrate transported. Specifically, Bisson et al. found that yeast transporters Gal2 and Hxt4 displayed 83.7% homology, but Gal2 appeared to transport galactose, while Hxt4 appeared to transport glucose (based on knockout phenotype, Tables 1 and 2). Similarly, Liang et al. (Mol. Cell. Biol. 18(2): 926-935, 1998) found that several single amino acid substitutions in yeast glucose transporters can change substrate specificity. Barrett et al. (Curr Opin Cell Biol 11(4) : 496-502, 1999) report that substitutions in *S. cerevisiae hxt1, hxt3*, and *gal2* genes render these mutant transporters glucose transport deficient (pg 497, col 2, last ¶). Mutation of Arg107 (Arg92 in Glut1), Arg349 (Arg 333 in Glut1), and Arg350 (Arg334 in Glut1) abrogates glucose transport but not binding, indicating a conformational change in the transporter (pg 500, col 1-2). Also, mutations of Glu162 (Glu146 in Glut1) and Arg169 (Arg153 in Glut1) are crucial for both ligand binding and transport (pg 500, col 2). Regarding the SLC22 family, which the claimed OCTN1 nucleic acid is a member, Koepsell et al. (Rev Physiol Biochem Pharmacol 150: 36-90, 2003; pg 70 and Figure 4) teach that certain mutations in OCTN2, OCT1, OAT1, and OAT3 may disturb targeting or regulation or may induce gross structural changes that alter targeting, regulation, and/or transport. Koepsell et al. also indicate that mutations in rOCT1, fOAT1, and rOAT3 change substrate specificity of these transporters (pg 70, 2nd full paragraph).

Due to the large quantity of experimentation necessary to generate the infinite number of variants and fragments recited in the claims and possibly screen same for activity; the lack of direction/guidance presented in the specification regarding which structural features are required

in order to provide activity; the absence of working examples directed to same; the complex nature of the invention; the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function; and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

8. Claims 8, 10-12, 14-16, 18-21, 23-25, and 27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to an isolated nucleic acid encoding a polypeptide comprising an amino acid sequence at least 70% identical to SEQ ID NO: 1, wherein the polypeptide is a transporter of an organic cation. The claims are also directed to an isolated nucleic acid encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 1, with up to 30 consecutive amino acid substitutions, wherein the polypeptide is a transporter of an organic cation. The claims recite an isolated nucleic acid comprising a strand that hybridizes under stringent conditions to a single stranded probe, the sequence of which consists of SEQ ID NO: 2 or the complement. The claims recite the strand is at least 15 nucleotides long. The claims also recite vectors, cultured host cells, and a method of producing a polypeptide.

The specification of the instant application teaches that mutant proteins obtained by altering the amino acid sequence of the transporter protein by substitution, deletion, or addition of amino acid residues and are functionally equivalent to those transporter proteins of the

invention are included in the invention (pg 9, lines 22-27). However, to provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved. Additionally, with regard to claim 11, simply reciting hybridization conditions in the claim does not yield adequate written description of the polynucleotides encompassed. The claim encompasses an infinite number of polynucleotides that hybridize to the nucleic acid sequence of SEQ ID NO: 2 or its complement. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. Additionally, the description of one polynucleotide species (SEQ ID NO: 2) and one polypeptide species (SEQ ID NO: 1) is not adequate written description of an entire genus of functionally equivalent polynucleotides which incorporate all polynucleotide variants and fragments that (1) encode a polypeptide at least 70% identical to SEQ ID NO: 1, (2) encode a polypeptide of SEQ ID NO: 1, with up to 30 conservative amino acid substitutions, and (3) hybridize to SEQ ID NO:2.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed"* (See page 1117). The specification does not "clearly allow persons of

ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

With the exception of the sequences referred to above (SEQ ID NOs: 1, 2), the skilled artisan cannot envision the detailed chemical structure of the encompassed nucleic acids, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The polynucleotide itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only an isolated nucleic acid encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 1 and an isolated nucleic acid consisting of the nucleic acid sequence of SEQ ID NO: 2, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 8-25 and 27 are rejected under 35 U.S.C. 102(a) as being anticipated by Tamai et al. (FEBS Lett 419: 107-111, 1997).

Tamai et al. teach an isolated nucleic acid encoding the organic transporter protein comprising the amino acid sequence of SEQ ID NO: 1 of the instant application (see pg 109, col 1 and Figure 1A of Tamai et al.; see also sequence alignment attached to the instant Office Action as Appendix A). Tamai et al. disclose that the cloned "OCTN1" cDNA consists of 2135 nucleotides and refers to Genbank Accession No. AB007448 (pg 109, col 1). The OCTN1 DNA sequence of Tamai et al. is 100% identical to SEQ ID NO: 2 of the instant application (see, for example, the sequence alignment attached to the instant Office Action as Appendix B). Tamai et al. disclose that OCTN1 has 11 putative membrane spanning domains, four N-glycosylation sites, five protein kinase C phosphorylation sites, a nucleotide binding site sequence motif, and a sugar transport protein signature (pg 109, col 1). Additionally, Tamai et al. teach that OCNT1 cDNA is subcloned into the expression vector pcDNA3 and transfected into HEK293 cells (pg 108, col 1). Tamai et al. teach that the cells are incubated with different compounds (such as TEA, sodium azide, and 3-0-methylglucose), the transport of TEA is measured, and cellular protein content is determined (pg 108, col 2; pg 109; pg 110, col 1).

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

10. Claim 11 is rejected under 35 U.S.C. 102(b) as being anticipated by Martin et al. (Genbank Accession No. HSL81760, 09 April 1997). It is noted that claim 11 has been interpreted by the Examiner as encompassing an infinite number of nucleic acids that hybridize to the nucleic acid sequence of SEQ ID NO: 2 because DNA will hybridize under conditions of low or no stringency.

Martin et al. teach an isolated nucleic acid sequence that hybridizes to the nucleic acid sequence of SEQ ID NO: 2 of the instant application (see nucleotides 1708-1170 of Martin et al. and nucleotides 1-539 of SEQ ID NO: 2; see sequence alignment attached to the instant Office Action as Appendix C).

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BEB
Art Unit 1647
07 August 2006

Bridget E. Bunner

BRIDGET BUNNER
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Brenda Brumback

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SUPERVISORY PATENT EXAMINER
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Appendix A

```
RESULT 3
AB007448
LOCUS       AB007448               2135 bp    mRNA    linear   PRI 13-FEB-1999
DEFINITION  Homo sapiens mRNA for OCTN1, complete cds.
ACCESSION   AB007448
VERSION     AB007448.1  GI:2605500
KEYWORDS    polyspecific oraganic cation transporter; fls631; OCTN1.
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini;
            Hominidae; Homo.
REFERENCE   1  (sites)
  AUTHORS   Tamai,I., Yabuuchi,H., Nezu,J., Sai,Y., Oku,A., Shimane,M. and
            Tsuji,A.
  TITLE     Cloning and characterization of a novel human pH-dependent organic
            cation transporter, OCTN1
  JOURNAL   FEBS Lett. 419 (1), 107-111 (1997)
   PUBMED   9426230
REFERENCE   2  (bases 1 to 2135)
  AUTHORS   Nezu,J.
  TITLE     Direct Submission
  JOURNAL   Submitted (18-SEP-1997) Jun-ichi Nezu, Chugai Research Institute
            for Molecular Medicine, Inc., Gene Search Program; 153-2 Nagai,
            Niihari, Ibaraki 300-4101, Japan (E-mail:nezuj@cimmed.com,
            Tel:81-298-30-6211, Fax:81-298-30-6270)
FEATURES             Location/Qualifiers
     source          1. .2135
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                     /gene="OCTN1"
     CDS             147. .1802
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                     RTLPRRYIIAAVLFWGGGVLLFIQLVPVDYYFLSIGLVMLGKFGITSAFSMLYVFTAE
                     LYPTLVRNMAVGVTSTASRVGSIIAPYFVYLGAYNRMLPYIVMGSLTVLIGIFTLFFP
                     ESLGMTLPETLEQMQKVKWFRSGKKTRDSMETEENPKVLITAF"
ORIGIN

Alignment Scores:
Pred. No.:              1.27e-284       Length:         2135
Score:                  2845.00         Matches:        551
Percent Similarity:     100.0%          Conservative:   0
Best Local Similarity:  100.0%          Mismatches:     0
Query Match:            100.0%          Indels:         0
DB:                     5               Gaps:           0

US-10-762-154-1 (1-551) x AB007448 (1-2135)

Qy          1 MetArgAspTyrAspGluValIleAlaPheLeuGlyGluTrpGlyProPheGlnArgLeu 20
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        147 ATGCGGGACTACGACGAGGTGATCGCCTTCCTGGGCGAGTGGGGGCCCTTCCAGCGCCTC 206

Qy         21 IlePhePheLeuLeuSerAlaSerIleIleProAsnGlyPheAsnGlyMetSerValVal 40
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        207 ATCTTCTTCCTGCTCAGCGCCAGCATCATCCCCAATGGCTTCAATGGTATGTCAGTCGTG 266

Qy         41 PheLeuAlaGlyThrProGluHisArgCysArgValProAspAlaAlaAsnLeuSerSer 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        267 TTCCTGGCGGGGACCCCGGAGCACCGCTGTCGAGTGCCGGACGCCGCGAACCTGAGCAGC 326

Qy         61 AlaTrpArgAsnAsnSerValProLeuArgLeuArgAspGlyArgGluValProHisSer 80
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        327 GCCTGGCGCAACAACAGTGTCCCGCTGCGGCTGCGGGACGGCCGCGAGGTGCCCCACAGC 386
```

Appendix A (cont.)

```
Qy        81 CysSerArgTyrArgLeuAlaThrIleAlaAsnPheSerAlaLeuGlyLeuGluProGly 100
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       387 TGCAGCCGCTACCGGCTCGCCACCATCGCCAACTTCTCGGCGCTCGGGCTGGAGCCGGGG 446

Qy       101 ArgAspValAspLeuGlyGlnLeuGluGlnGluSerCysLeuAspGlyTrpGluPheSer 120
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       447 CGCGACGTGGACCTGGGGCAGCTGGAGCAGGAGAGCTGCCTGGATGGCTGGGAGTTCAGC 506

Qy       121 GlnAspValTyrLeuSerThrValValThrGluTrpAsnLeuValCysGluAspAsnTrp 140
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       507 CAGGACGTCTACCTGTCCACCGTCGTGACCGAGTGGAATCTGGTGTGTGAGGACAACTGG 566

Qy       141 LysValProLeuThrThrSerLeuPhePheValGlyValLeuLeuGlySerPheValSer 160
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       567 AAGGTGCCCCTCACCACCTCCCTGTTCTTCGTAGGCGTGCTCCTCGGCTCCTTCGTGTCC 626

Qy       161 GlyGlnLeuSerAspArgPheGlyArgLysAsnValLeuPheAlaThrMetAlaValGln 180
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       627 GGGCAGCTGTCAGACAGGTTTGGCAGGAAGAACGTTCTCTTCGCAACCATGGCTGTACAG 686

Qy       181 ThrGlyPheSerPheLeuGlnIlePheSerIleSerTrpGluMetPheThrValLeuPhe 200
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       687 ACTGGCTTCAGCTTCCTGCAGATTTTCTCCATCAGCTGGGAGATGTTCACTGTGTTATTT 746

Qy       201 ValIleValGlyMetGlyGlnIleSerAsnTyrValValAlaPheIleLeuGlyThrGlu 220
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       747 GTCATCGTGGGCATGGGCCAGATCTCCAACTATGTGGTAGCCTTCATACTAGGAACAGAA 806

Qy       221 IleLeuGlyLysSerValArgIleIlePheSerThrLeuGlyValCysThrPhePheAla 240
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       807 ATTCTTGGCAAGTCAGTTCGTATTATATTCTCTACATTAGGAGTGTGCACATTTTTTGCA 866

Qy       241 ValGlyTyrMetLeuLeuProLeuPheAlaTyrPheIleArgAspTrpArgMetLeuLeu 260
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       867 GTTGGCTATATGCTGCTGCCACTGTTTGCTTACTTCATCAGAGACTGGCGGATGCTGCTG 926

Qy       261 LeuAlaLeuThrValProGlyValLeuCysValProLeuTrpTrpPheIleProGluSer 280
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       927 CTGGCGCTGACGGTGCCGGGAGTGCTGTGTGTCCCGCTGTGGTGGTTCATTCCTGAATCT 986

Qy       281 ProArgTrpLeuIleSerGlnArgArgPheArgGluAlaGluAspIleIleGlnLysAla 300
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       987 CCCCGATGGCTGATATCCCAGAGAAGATTTAGAGAGGCTGAAGATATCATCCAAAAAGCT 1046

Qy       301 AlaLysMetAsnAsnThrAlaValProAlaValIlePheAspSerValGluGluLeuAsn 320
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1047 GCAAAAATGAACAACACAGCTGTACCAGCAGTGATATTTGATTCTGTGGAGGAGCTAAAT 1106

Qy       321 ProLeuLysGlnGlnLysAlaPheIleLeuAspLeuPheArgThrArgAsnIleAlaIle 340
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1107 CCCCTGAAGCAGCAGAAAGCTTTCATTCTGGACCTGTTCAGGACTCGGAATATTGCCATA 1166

Qy       341 MetThrIleMetSerLeuLeuLeuTrpMetLeuThrSerValGlyTyrPheAlaLeuSer 360
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1167 ATGACCATTATGTCTTTGCTGCTATGGATGCTGACCTCAGTGGGTTACTTTGCTCTGTCT 1226

Qy       361 LeuAspAlaProAsnLeuHisGlyAspAlaTyrLeuAsnCysPheLeuSerAlaLeuIle 380
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1227 CTGGATGCTCCTAATTTACATGGAGATGCCTACCTGAACTGTTTCCTCTCTGCCTTGATT 1286

Qy       381 GluIleProAlaTyrIleThrAlaTrpLeuLeuLeuArgThrLeuProArgArgTyrIle 400
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1287 GAAATTCCAGCTTACATTACAGCCTGGCTGCTATTGCGAACGCTGCCCAGGCGTTATATC 1346

Qy       401 IleAlaAlaValLeuPheTrpGlyGlyGlyValLeuLeuPheIleGlnLeuValProVal 420
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1347 ATAGCTGCAGTACTGTTCTGGGGAGGAGGTGTGCTTCTCTTCATTCAACTGGTACCTGTG 1406

Qy       421 AspTyrTyrPheLeuSerIleGlyLeuValMetLeuGlyLysPheGlyIleThrSerAla 440
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1407 GATTATTACTTCTTATCCATTGGTCTGGTCATGCTGGGAAAATTTGGGATCACCTCTGCT 1466

Qy       441 PheSerMetLeuTyrValPheThrAlaGluLeuTyrProThrLeuValArgAsnMetAla 460
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1467 TTCTCCATGCTGTATGTCTTCACTGCTGAGCTCTACCCAACCCTGGTCAGGAACATGGCG 1526

Qy       461 ValGlyValThrSerThrAlaSerArgValGlySerIleIleAlaProTyrPheValTyr 480
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1527 GTGGGGGTCACATCCACGGCCTCCAGAGTGGGCAGCATCATTGCCCCCTACTTTGTTTAC 1586
```

Appendix A (cont.)

```
Qy        481 LeuGlyAlaTyrAsnArgMetLeuProTyrIleValMetGlySerLeuThrValLeuIle 500
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1587 CTCGGTGCTTACAACAGAATGCTGCCCTACATCGTCATGGGTAGTCTGACTGTCCTGATT 1646

Qy        501 GlyIlePheThrLeuPhePheProGluSerLeuGlyMetThrLeuProGluThrLeuGlu 520
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1647 GGAATCTTCACCCTTTTTTTCCCTGAAAGTTTGGGAATGACTCTTCCAGAAACCTTAGAG 1706

Qy        521 GlnMetGlnLysValLysTrpPheArgSerGlyLysLysThrArgAspSerMetGluThr 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1707 CAGATGCAGAAAGTGAAATGGTTCAGATCTGGGAAAAAAACAAGAGACTCAATGGAGACA 1766

Qy        541 GluGluAsnProLysValLeuIleThrAlaPhe 551
              |||||||||||||||||||||||||||||||
Db       1767 GAAGAAAATCCCAAGGTTCTAATAACTGCATTC 1799
```

Appendix B

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RESULT 3
AB007448
LOCUS       AB007448               2135 bp    mRNA    linear   PRI 13-FEB-1999
DEFINITION  Homo sapiens mRNA for OCTN1, complete cds.
ACCESSION   AB007448
VERSION     AB007448.1  GI:2605500
KEYWORDS    polyspecific oraganic cation transporter; fls631; OCTN1.
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini;
            Hominidae; Homo.
REFERENCE   1  (sites)
  AUTHORS   Tamai,I., Yabuuchi,H., Nezu,J., Sai,Y., Oku,A., Shimane,M. and
            Tsuji,A.
  TITLE     Cloning and characterization of a novel human pH-dependent organic
            cation transporter, OCTN1
  JOURNAL   FEBS Lett. 419 (1), 107-111 (1997)
   PUBMED   9426230
REFERENCE   2  (bases 1 to 2135)
  AUTHORS   Nezu,J.
  TITLE     Direct Submission
  JOURNAL   Submitted (18-SEP-1997) Jun-ichi Nezu, Chugai Research Institute
            for Molecular Medicine, Inc., Gene Search Program; 153-2 Nagai,
            Niihari, Ibaraki 300-4101, Japan (E-mail:nezuj@cimmed.com,
            Tel:81-298-30-6211, Fax:81-298-30-6270)
FEATURES             Location/Qualifiers
     source          1. .2135
                     /organism="Homo sapiens"
                     /mol_type="mRNA"
                     /db_xref="taxon:9606"
                     /chromosome="5"
                     /tissue_type="liver"
                     /dev_stage="fetal"
                     /note="inbetween D5S642 and D5S649"
     gene            1. .2135
                     /gene="OCTN1"
     CDS             147. .1802
                     /gene="OCTN1"
                     /note="oraganic cation transporter OCTN1 (fls631)"
                     /codon_start=1
                     /product="OCTN1"
                     /protein_id="BAA23356.1"
                     /db_xref="GI:2605501"
                     /translation="MRDYDEVIAFLGEWGPFQRLIFFLLSASIIPNGFNGMSVVFLAG
                     TPEHRCRVPDAANLSSAWRNNSVPLRLRDGREVPHSCSRYRLATIANFSALGLEPGRD
                     VDLGQLEQESCLDGWEFSQDVYLSTVVTEWNLVCEDNWKVPLTTSLFFVGVLLGSFVS
                     GQLSDRFGRKNVLFATMAVQTGFSFLQIFSISWEMFTVLFVIVGMGQISNYVVAFILG
                     TEILGKSVRIIFSTLGVCTFFAVGYMLLPLFAYFIRDWRMLLLALTVPGVLCVPLWWF
                     IPESPRWLISQRRFREAEDIIQKAAKMNNTAVPAVIFDSVEELNPLKQQKAFILDLFR
                     TRNIAIMTIMSLLLWMLTSVGYFALSLDAPNLHGDAYLNCFLSALIEIPAYITAWLLL
                     RTLPRRYIIAAVLFWGGGVLLFIQLVPVDYYFLSIGLVMLGKFGITSAFSMLYVFTAE
                     LYPTLVRNMAVGVTSTASRVGSIIAPYFVYLGAYNRMLPYIVMGSLTVLIGIFTLFFP
                     ESLGMTLPETLEQMQKVKWFRSGKKTRDSMETEENPKVLITAF"
ORIGIN

  Query Match             100.0%;  Score 2135;  DB 5;  Length 2135;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2135;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 CCCCGGCTTCGCGCCCCAATTTCTAACAGCCTGCCTGTCCCCCGGGAACGTTCTAACATC 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 CCCCGGCTTCGCGCCCCAATTTCTAACAGCCTGCCTGTCCCCCGGGAACGTTCTAACATC 60

Qy         61 CTTGGGGAGCGCCCCAGCTACAAGACACTGTCCTGAGAACGCTGTCATCACCCGTAGTTG 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 CTTGGGGAGCGCCCCAGCTACAAGACACTGTCCTGAGAACGCTGTCATCACCCGTAGTTG 120

Qy        121 CAAGTTTCGGAGCGGCAGTGGGAAGCATGCGGGACTACGACGAGGTGATCGCCTTCCTGG 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 CAAGTTTCGGAGCGGCAGTGGGAAGCATGCGGGACTACGACGAGGTGATCGCCTTCCTGG 180

Qy        181 GCGAGTGGGGGCCCTTCCAGCGCCTCATCTTCTTCCTGCTCAGCGCCAGCATCATCCCCA 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 GCGAGTGGGGGCCCTTCCAGCGCCTCATCTTCTTCCTGCTCAGCGCCAGCATCATCCCCA 240

Qy        241 ATGGCTTCAATGGTATGTCAGTCGTGTTCCTGGCGGGGACCCCGGAGCACCGCTGTCGAG 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 ATGGCTTCAATGGTATGTCAGTCGTGTTCCTGGCGGGGACCCCGGAGCACCGCTGTCGAG 300

Qy        301 TGCCGGACGCCGCGAACCTGAGCAGCGCCTGGCGCAACAACAGTGTCCCGCTGCGGCTGC 360
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Appendix B (cont.)

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                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 TGCCGGACGCCGCGAACCTGAGCAGCGCCTGGCGCAACAACAGTGTCCCGCTGCGGCTGC 360

Qy        361 GGGACGGCCGCGAGGTGCCCCACAGCTGCAGCCGCTACCGGCTCGCCACCATCGCCAACT 420
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 GGGACGGCCGCGAGGTGCCCCACAGCTGCAGCCGCTACCGGCTCGCCACCATCGCCAACT 420

Qy        421 TCTCGGCGCTCGGGCTGGAGCCGGGGCGCGACGTGGACCTGGGGCAGCTGGAGCAGGAGA 480
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 TCTCGGCGCTCGGGCTGGAGCCGGGGCGCGACGTGGACCTGGGGCAGCTGGAGCAGGAGA 480

Qy        481 GCTGCCTGGATGGCTGGGAGTTCAGCCAGGACGTCTACCTGTCCACCGTCGTGACCGAGT 540
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 GCTGCCTGGATGGCTGGGAGTTCAGCCAGGACGTCTACCTGTCCACCGTCGTGACCGAGT 540

Qy        541 GGAATCTGGTGTGTGAGGACAACTGGAAGGTGCCCCTCACCACCTCCCTGTTCTTCGTAG 600
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 GGAATCTGGTGTGTGAGGACAACTGGAAGGTGCCCCTCACCACCTCCCTGTTCTTCGTAG 600

Qy        601 GCGTGCTCCTCGGCTCCTTCGTGTCCGGGCAGCTGTCAGACAGGTTTGGCAGGAAGAACG 660
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 GCGTGCTCCTCGGCTCCTTCGTGTCCGGGCAGCTGTCAGACAGGTTTGGCAGGAAGAACG 660

Qy        661 TTCTCTTCGCAACCATGGCTGTACAGACTGGCTTCAGCTTCCTGCAGATTTTCTCCATCA 720
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 TTCTCTTCGCAACCATGGCTGTACAGACTGGCTTCAGCTTCCTGCAGATTTTCTCCATCA 720

Qy        721 GCTGGGAGATGTTCACTGTGTTATTTGTCATCGTGGGCATGGGCCAGATCTCCAACTATG 780
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 GCTGGGAGATGTTCACTGTGTTATTTGTCATCGTGGGCATGGGCCAGATCTCCAACTATG 780

Qy        781 TGGTAGCCTTCATACTAGGAACAGAAATTCTTGGCAAGTCAGTTCGTATTATATTCTCTA 840
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 TGGTAGCCTTCATACTAGGAACAGAAATTCTTGGCAAGTCAGTTCGTATTATATTCTCTA 840

Qy        841 CATTAGGAGTGTGCACATTTTTTGCAGTTGGCTATATGCTGCTGCCACTGTTTGCTTACT 900
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 CATTAGGAGTGTGCACATTTTTTGCAGTTGGCTATATGCTGCTGCCACTGTTTGCTTACT 900

Qy        901 TCATCAGAGACTGGCGGATGCTGCTGCTGGCGCTGACGGTGCCGGGAGTGCTGTGTGTCC 960
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 TCATCAGAGACTGGCGGATGCTGCTGCTGGCGCTGACGGTGCCGGGAGTGCTGTGTGTCC 960

Qy        961 CGCTGTGGTGGTTCATTCCTGAATCTCCCCGATGGCTGATATCCCAGAGAAGATTTAGAG 1020
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 CGCTGTGGTGGTTCATTCCTGAATCTCCCCGATGGCTGATATCCCAGAGAAGATTTAGAG 1020

Qy       1021 AGGCTGAAGATATCATCCAAAAAGCTGCAAAAATGAACAACACAGCTGTACCAGCAGTGA 1080
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 AGGCTGAAGATATCATCCAAAAAGCTGCAAAAATGAACAACACAGCTGTACCAGCAGTGA 1080

Qy       1081 TATTTGATTCTGTGGAGGAGCTAAATCCCCTGAAGCAGCAGAAAGCTTTCATTCTGGACC 1140
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 TATTTGATTCTGTGGAGGAGCTAAATCCCCTGAAGCAGCAGAAAGCTTTCATTCTGGACC 1140

Qy       1141 TGTTCAGGACTCGGAATATTGCCATAATGACCATTATGTCTTTGCTGCTATGGATGCTGA 1200
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 TGTTCAGGACTCGGAATATTGCCATAATGACCATTATGTCTTTGCTGCTATGGATGCTGA 1200

Qy       1201 CCTCAGTGGGTTACTTTGCTCTGTCTCTGGATGCTCCTAATTTACATGGAGATGCCTACC 1260
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 CCTCAGTGGGTTACTTTGCTCTGTCTCTGGATGCTCCTAATTTACATGGAGATGCCTACC 1260

Qy       1261 TGAACTGTTTCCTCTCTGCCTTGATTGAAATTCCAGCTTACATTACAGCCTGGCTGCTAT 1320
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 TGAACTGTTTCCTCTCTGCCTTGATTGAAATTCCAGCTTACATTACAGCCTGGCTGCTAT 1320

Qy       1321 TGCGAACGCTGCCCAGGCGTTATATCATAGCTGCAGTACTGTTCTGGGGAGGAGGTGTGC 1380
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 TGCGAACGCTGCCCAGGCGTTATATCATAGCTGCAGTACTGTTCTGGGGAGGAGGTGTGC 1380

Qy       1381 TTCTCTTCATTCAACTGGTACCTGTGGATTATTACTTCTTATCCATTGGTCTGGTCATGC 1440
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 TTCTCTTCATTCAACTGGTACCTGTGGATTATTACTTCTTATCCATTGGTCTGGTCATGC 1440

Qy       1441 TGGGAAAATTTGGGATCACCTCTGCTTTCTCCATGCTGTATGTCTTCACTGCTGAGCTCT 1500
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 TGGGAAAATTTGGGATCACCTCTGCTTTCTCCATGCTGTATGTCTTCACTGCTGAGCTCT 1500

Qy       1501 ACCCAACCCTGGTCAGGAACATGGCGGTGGGGGTCACATCCACGGCCTCCAGAGTGGGCA 1560
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
```

Appendix B (cont.)

```
Db      1501 ACCCAACCCTGGTCAGGAACATGGCGGTGGGGGTCACATCCACGGCCTCCAGAGTGGGCA 1560

Qy      1561 GCATCATTGCCCCCTACTTTGTTTACCTCGGTGCTTACAACAGAATGCTGCCCTACATCG 1620
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1561 GCATCATTGCCCCCTACTTTGTTTACCTCGGTGCTTACAACAGAATGCTGCCCTACATCG 1620

Qy      1621 TCATGGGTAGTCTGACTGTCCTGATTGGAATCTTCACCCTTTTTTTCCCTGAAAGTTTGG 1680
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1621 TCATGGGTAGTCTGACTGTCCTGATTGGAATCTTCACCCTTTTTTTCCCTGAAAGTTTGG 1680

Qy      1681 GAATGACTCTTCCAGAAACCTTAGAGCAGATGCAGAAAGTGAAATGGTTCAGATCTGGGA 1740
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1681 GAATGACTCTTCCAGAAACCTTAGAGCAGATGCAGAAAGTGAAATGGTTCAGATCTGGGA 1740

Qy      1741 AAAAAACAAGAGACTCAATGGAGACAGAAGAAAATCCCAAGGTTCTAATAACTGCATTCT 1800
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1741 AAAAAACAAGAGACTCAATGGAGACAGAAGAAAATCCCAAGGTTCTAATAACTGCATTCT 1800

Qy      1801 GAAAAAATATCTACCCCATTTGGTGAAGTGAAAAACAGAAAAATAAGACCCTGTGGAGAA 1860
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1801 GAAAAAATATCTACCCCATTTGGTGAAGTGAAAAACAGAAAAATAAGACCCTGTGGAGAA 1860

Qy      1861 ATTCGTTGTTCCCACTGAAATGGACTGACTGTAACGATTGACACCAAAATGAACCTTGCT 1920
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1861 ATTCGTTGTTCCCACTGAAATGGACTGACTGTAACGATTGACACCAAAATGAACCTTGCT 1920

Qy      1921 ATCAAGAAATGCTCGTCATACAGTAAACTCTGGATGATTCTTCCAGATAATGTCCTTGCT 1980
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1921 ATCAAGAAATGCTCGTCATACAGTAAACTCTGGATGATTCTTCCAGATAATGTCCTTGCT 1980

Qy      1981 TTACAAACCAACCATTTCTAGAGAGTCTCCTTACTCATTAATTCAATGAAATGGATTGGT 2040
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1981 TTACAAACCAACCATTTCTAGAGAGTCTCCTTACTCATTAATTCAATGAAATGGATTGGT 2040

Qy      2041 AAGATGTCTTGAAAACATGTTAGTCAAGGACTGGTAAAATACATATAAAGATTAACACTC 2100
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      2041 AAGATGTCTTGAAAACATGTTAGTCAAGGACTGGTAAAATACATATAAAGATTAACACTC 2100

Qy      2101 ATTTCCAATCATACAAATACTATCCAAATAAAAAT 2135
             |||||||||||||||||||||||||||||||||||
Db      2101 ATTTCCAATCATACAAATACTATCCAAATAAAAAT 2135
```

>gi|1930518|gb|L81760.1|HSL81760 Homo sapiens (subclone 6_c8 from P1 H17) DNA sequence, comp] sequence
Length=3081

Appendix C

Score = 1068 bits (539), Expect = 0.0
Identities = 539/539 (100%), Gaps = 0/539 (0%)
Strand=Plus/Minus

```
Query  1     CCCCGGCTTCGCGCCCCAATTTCTAACAGCCTGCCTGTCCCCCGGGAACGTTCTAACATC  60
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  1708  CCCCGGCTTCGCGCCCCAATTTCTAACAGCCTGCCTGTCCCCCGGGAACGTTCTAACATC  1649

Query  61    CTTGGGGAGCGCCCCAGCTACAAGACACTGTCCTGAGAACGCTGTCATCACCCGTAGTTG  120
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  1648  CTTGGGGAGCGCCCCAGCTACAAGACACTGTCCTGAGAACGCTGTCATCACCCGTAGTTG  1589

Query  121   CAAGTTTCGGAGCGGCAGTGGGAAGCATGCGGGACTACGACGAGGTGATCGCCTTCCTGG  180
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  1588  CAAGTTTCGGAGCGGCAGTGGGAAGCATGCGGGACTACGACGAGGTGATCGCCTTCCTGG  1529

Query  181   GCGAGTGGGGGCCCTTCCAGCGCCTCATCTTCTTCCTGCTCAGCGCCAGCATCATCCCCA  240
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  1528  GCGAGTGGGGGCCCTTCCAGCGCCTCATCTTCTTCCTGCTCAGCGCCAGCATCATCCCCA  1469

Query  241   ATGGCTTCAATGGTATGTCAGTCGTGTTCCTGGCGGGGACCCCGGAGCACCGCTGTCGAG  300
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  1468  ATGGCTTCAATGGTATGTCAGTCGTGTTCCTGGCGGGGACCCCGGAGCACCGCTGTCGAG  1409

Query  301   TGCCGGACGCCGCGAACCTGAGCAGCGCCTGGCGCAACAACAGTGTCCCGCTGCGGCTGC  360
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  1408  TGCCGGACGCCGCGAACCTGAGCAGCGCCTGGCGCAACAACAGTGTCCCGCTGCGGCTGC  1349

Query  361   GGGACGGCCGCGAGGTGCCCCACAGCTGCAGCCGCTACCGGCTCGCCACCATCGCCAACT  420
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  1348  GGGACGGCCGCGAGGTGCCCCACAGCTGCAGCCGCTACCGGCTCGCCACCATCGCCAACT  1289

Query  421   TCTCGGCGCTCGGGCTGGAGCCGGGGCGCGACGTGGACCTGGGGCAGCTGGAGCAGGAGA  480
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  1288  TCTCGGCGCTCGGGCTGGAGCCGGGGCGCGACGTGGACCTGGGGCAGCTGGAGCAGGAGA  1229

Query  481   GCTGCCTGGATGGCTGGGAGTTCAGCCAGGACGTCTACCTGTCCACCGTCGTGACCGAG  539
             |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  1228  GCTGCCTGGATGGCTGGGAGTTCAGCCAGGACGTCTACCTGTCCACCGTCGTGACCGAG  1170
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